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# Epidemiology and clinical features of *Mycoplasma pneumoniae* infection in children

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## KEYWORDS

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## Summary

*Mycoplasma pneumoniae* (MP) is, considered to affect rarely children less than 5 yrs of age. This study was performed to describe the epidemiology and the clinical features of MP lower respiratory tract infection (LRTI) in children, presenting to a tertiary children hospital.

Eleven month-longitudinal study of LRTI due to MP, diagnosed by polymerase chain reaction (PCR) on throat swab specimen, was performed.

Out of 866 children with LRTI admitted to the Gaslini Pediatric Institute in Genoa, 102 had a positive PCR for MP. We found 39 preschool-aged children, 42 school-aged children and 21 young adolescent [6.20 (3.81) yrs old]. Interestingly, eight MP+ infants had <8 months of age. The commonest presentations were cough and/or fever (76.5%). Tachypnoea, upper respiratory tract involvement, diarrhoea and vomiting were more common in the <5 yr Gr as compared to the other groups. Chest X-ray was found abnormal in 76 children: consolidations were the commonest finding. Laboratory test showed that the preschool-aged children had a higher number of lymphocytes ( $p < 0.0001$ ) and monocytes ( $p = 0.009$ ). Thrombocytosis was found in 35.7% of children and was more frequent in the preschool-aged children ( $p = 0.013$ ).

MP infection is common in preschool-aged children, including young infants, and may have different clinical presentation, as compared to older children.

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## Introduction

Mycoplasmas, the smallest known free-living forms, have been associated with a variety of clinical manifestations, including those involving the respiratory tract which are related to *Mycoplasma pneumoniae* (*M. pneumoniae*).<sup>1,2</sup> Indeed, *M. pneumoniae* is a significant cause of respiratory tract infections in humans and an important pathogen in acute respiratory illnesses in children and in adults, accounting for as many as 20–40% of all cases of community-acquired pneumonia.<sup>2–4</sup>

However, as direct invasion of the different tissues or, indirectly, as a result of the host immune system reaction to infection, *M. pneumoniae* can also cause extrapulmonary disorders affecting the skin, the gastrointestinal tract, the cardiovascular, musculoskeletal, nervous and renal systems.<sup>1–4</sup>

Current concepts recognize that community-acquired epidemics due to *M. pneumoniae* infection affect mainly school-aged children and young adults.<sup>2–5</sup> The assumption that *M. pneumoniae* disease is rare in preschool-aged children may probably precluded most physicians from considering it in the differential diagnosis in this age population. However, in the last decades studies indicated that *M. pneumoniae* infection may be frequent in children less than 5 yrs old, and suggested differences in its clinical presentation between younger and older patients.<sup>6–9</sup>

Evaluating paediatric patients with community-acquired pneumonia in Finland, it was found that out of the children with a confirmed diagnoses of *M. pneumoniae* infection, 21% were <5 yrs of age,<sup>6</sup> while during an epidemic outbreak of *M. pneumoniae* infection in Catalonia, rate in children <5 yrs old was 18% versus 8.2% in those 5–14 yrs old.<sup>7</sup> In contrast, evaluating the prevalence of *M. pneumoniae* in children in Turkey, detection of serum specific IgG was positive only in children >2 yrs old, with a sudden increase in seropositivity at 7 yrs of age.<sup>8</sup> Finally, the age group most commonly affected by *M. pneumoniae* infection in children presenting to a tertiary children's hospital in Australia was 5–9 yrs, followed by children of 1–5 yrs old.<sup>9</sup> Even though the commonest presentation in this study population was with cough and fever, coryza, diarrhoea, vomiting, tachypnoea and recession were significantly more common in children less than 5 yrs than in children 5–15 yrs.<sup>9</sup>

Due to the non homogeneous and limited data in the literature an 11-month-longitudinal study was performed to evaluate the epidemiology, the clinical and roentgenographic features and the laboratory results of *M. pneumoniae* lower respiratory tract infection (LRTI) in children, presenting to a tertiary children's hospital, aimed to evaluate possible age-related difference in the presenting clinical features.

## Materials and methods

### Study population

Eight hundred and eighty-six consecutive children with lower respiratory tract infection (LRTSI) admitted to the Gaslini Institute in Genoa were evaluated prospectively over a an 11-month period (October 1, 2005–August 31,

2006). Children were eligible for enrolment if they had: (a) clinical (fever, persistent cough, tachypnoea, chest retractions, or abnormal auscultatory findings) and/or radiologic evidence of LRTI (presence of consolidation, interstitial changes, pleural effusion or mediastinal lymphadenopathy) and (b) positive PCR and elevated IgM at admission or at follow-up or a fourfold increase in IgG.

For this research, fever was defined as a recorded temperature  $\geq 38.0^{\circ}\text{C}$  on admission.

Children were excluded if they had severe concomitant disease such as kidney or liver disease, neoplasms, primary ciliary dyskinesia, cystic fibrosis, congenital or acquired immunodeficiency or immunosuppression, due to systemic disorders, or treatments, cardiovascular disease or malabsorption syndromes.

According to the clinical findings, children were diagnosed as: (a) acute bronchitis, with or without wheezing, if they had cough and rhonchi, with a normal chest radiograph, when performed; (b) wheezy bronchitis if they had cough, and/or dyspnoea with expiratory rales and/or wheezes unrelated to any known specific sensitization, with a normal chest radiograph or hyperinflation, when performed; (c) pneumonia if they had diffuse or lobar pulmonary infiltration evident on the chest radiograph; (d) bronchiolitis when wheezing and/or dyspnoea and/or tachypnoea, and roentgenographic evidence of hyperinflation of the lung with or without areas of collapse were present.<sup>5,10,11</sup>

### Patient evaluation

Demographic and clinical data were collected uniformly from all children and laboratory specimens were obtained. These included nasal and throat swab specimens and blood samples cultured and processed in accordance with standard microbiological procedures for bacteria and the most common respiratory viruses. Blood samples were evaluated also for total cells and differential counts and serum level of C-reactive protein (CRP). Chest X-ray were was performed when clinically indicated. Diagnosis of *M. pneumoniae* infection was based on real-time PCR by targeting the P1 cytoadhesin type 1 and 2 gene of the *M. pneumoniae* genome using DNA extracted from oropharyngeal swabs. The swabs, stored in 1 ml of sterile PBS, were centrifuged at 14,000 rpm for 10 min and the pellets were resuspended in 200  $\mu\text{l}$  of PBS and processed to extract DNA with QIAamp DNA Mini kit (QIAGEN S.p.A., Milano, Italy). The PCR reaction was performed on samples and on positive and negative controls as follows: the 72 bp fragment of the target gene was amplified using Mycpn P1-F forward primer (5'-GCC GCA AAG ATG AAY GAC G-3') and Mycpn P1-F reverse primer (5'-TCC TTC CCC ATC TAA CAG TTC AG-3') in combination with a TaqMan probe (5'-FAM-TTG ATG GTA TTG TAC GCA CCC CAC TCG-3' TAMRA). Reaction was carried out with the Rotor Gene 3000 (Corbett Research, Diatech SRL, Italy) instrument. Each reaction mixture was performed in 25  $\mu\text{l}$  containing template DNA, 1 $\times$  Platinum Quantitative PCR SuperMix-UDG Master Mix (Invitrogen, Milano, Italy), primers at 300 nM and probe at 200 nM. PCR cycling conditions were 2 min at 50  $^{\circ}\text{C}$ , 2 min at 95  $^{\circ}\text{C}$  and then 40 cycles of denaturation at 95  $^{\circ}\text{C}$  for 20 s and annealing/extension 58  $^{\circ}\text{C}$  for 60 s.<sup>12–15</sup> PCR results were

available within 3 h. Acute IgM serology and/or elevated IgG titers in serum were also evaluated using a commercial test kit (Serion ELISA classic *M. pneumoniae* IgG/IgM, Institut Virion\Serion GmbH, Friedrich-Bergius-Ring 19 97076 Würzburg, Germany). IgM and IgG levels for *M. pneumoniae* were also re-evaluated 3–4 to weeks later, in “convalescence phase”, in patients with IgM < 30 U/ml and IgG < 17 U/ml.

The Institutional Ethical Committee of the Gaslini Institute approved the protocol. Signed informed parental consent were obtained.

## Data analysis

Descriptive statistics were performed and reported in terms of absolute frequencies or percentages for qualitative data, in terms of means or medians with standard deviations (SD) or lower and upper quartiles in parenthesis for quantitative data. Quantitative variables such as white blood cells, platelet count and oxygen saturation less in room air were dichotomized on the basis of the their ‘normal’ values related to different ages. Comparison of quantitative variables among the three age groups of patients was made by ANOVA or Kruskal–Wallis test when appropriate. Comparison of frequency distribution was made by means of the Chi-Square test, and the Fisher’s exact test was used in case of at least one expected frequency less than 5. All tests were two-tailed. Data were analysed using STATA version 7.0. A difference of  $P < 0.05$  was considered to be statistically significant.

## Results

### Patients

Out of the eight hundred and eighty-six children admitted for an acute respiratory disease, 102 (12%) had a positive PCR for *M. pneumoniae* and, of those, 63 (62.2%) had also antigen-specific IgM and/or antigen-specific IgG levels in the serum. The male to female ratio of the patients with *M. pneumoniae* infection (PCR positive) was 1.17 and the mean age was 6.20 (3.81) yrs, ranging from 1 month to 13.5 yrs. Subdividing the *M. pneumoniae* positive children into 3 age groups, we found 21 (20.6%) young adolescent (i.e.  $\geq 10$ – $\leq 14$  yrs old), 42 (41.2%) school-aged children (i.e.  $> 5$ – $< 10$  yr) and 39 (38.2%) preschool-aged children (i.e.  $< 5$  yr). In this latter group, 22 (21.57%) children were less than 24 months (Fig. 1). The mean hospital stay was 4.82 (2.68) while the treatment duration with macrolides (chlarytromycin) was  $11 \pm 2$  days.

Infection associated with *M. pneumoniae* occurred throughout the year, with 9 cases seen in most of the months. A peak was observed in June with a total of 23 (22.5%) cases seen during that period of the year (Fig. 2).

### Clinical presentation

#### Respiratory manifestations

The predominant onset symptoms were fever, [75 (73.5%)] and cough [43 (42.1%)]. Usually children reported the presence of persistent cough and fever, insensitive to beta-lactam antibiotics treatment. Cough was most

frequently described as moist, although a dry, non-productive cough was also described. In some patients, symptoms began abruptly with respiratory distress, with an oxygen saturation less than 95% in room air, detected in 36 (35.3%) children; none of these patients required assisted ventilation. Dyspnoea was detected in 28 children (27.5%). On physical examination children were found to have mild-to-moderate expiratory wheeze and inspiratory and expiratory crackles.

Although the respiratory system was always predominantly involved, twenty patients also had significant gastroenterologic manifestations, such as vomiting [15 (14.7%)] and diarrhoea [5 (4.9%)]. Two patients had a history of diffuse macular rash during illness involving the trunk and limbs and 2 patients of arthralgia while none presented haemolytic anaemia or symptoms suggesting nervous system involvement. Comparison among the three age groups, showed that dyspnoea, upper respiratory tract involvement, diarrhoea and vomiting were more common in the preschool-aged group (38.46%) as compared to the older groups (14.29% in school-aged children and 28.57% in young adolescents) ( $p = 0.047$ ). Similarly, we also observed that dyspnoea was more frequently diagnosed in preschool-aged children than in older children (Table 1). Among the 102 patients evaluated, 6 (5.89%) had a previous diagnosis of asthma and 42 (41.18%) had previous history of upper and/or lower respiratory tract infections.

### Investigations

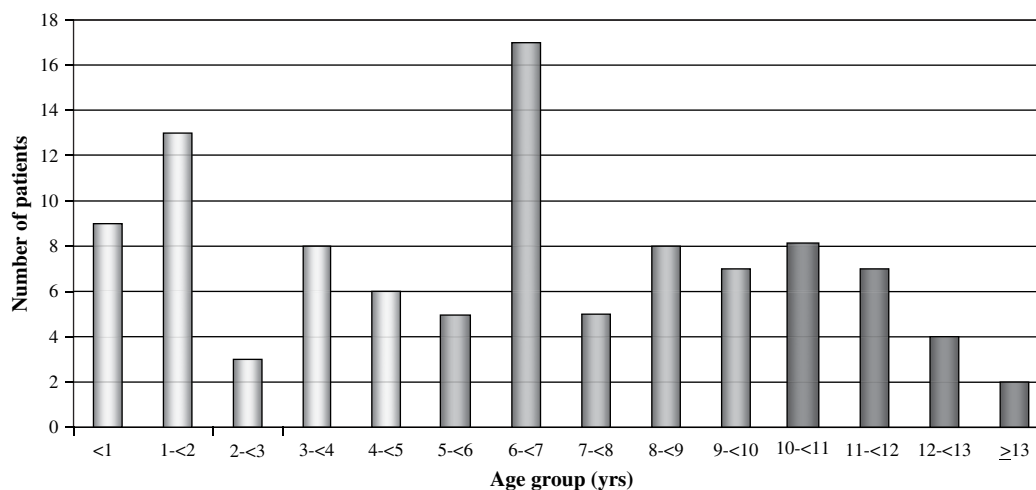
A chest X-ray was performed in 81 of the 102 children. Seventy-six roentgenograms (93.8%) were reported as abnormal. Consolidation was the commonest finding, in 62 (76.5%) of the radiological abnormalities recorded, more often unilateral (53.09%) than bilateral (23.46%). Interstitial changes were reported in 14 patients (17.28%), and pleural effusion in 6 (7.4%). Mediastinal lymphadenopathy was never detected.

On the basis of both clinical and roentgenographic findings, a diagnosis of pneumonia with or without pleural effusion was done in 77 children, acute bronchitis in four, wheezy bronchitis in 18 and bronchiolitis in three.

Interstitial changes were more frequently reported in preschool-aged group than in school-aged or young adolescent groups ( $p < 0.0001$ , Table 1) whereas consolidations were more frequently reported in the 5– $< 10$  yrs and  $\geq 10$  yrs groups than in  $< 5$  yrs group ( $p = 0.004$ ) (Table 1).

A full blood count was available in all patients. Total WBC count varied from  $3.33 \times 10^3$  to  $26.56 \times 10^3$  cells/mm<sup>3</sup> (mean  $11.22 \times 10^3$  cells/mm<sup>3</sup>). Normal leukocyte total and differential count, was found in 82 patients (81%). Twenty children (19%) had leukocytosis. Thrombocytosis, defined as a platelet count more than  $400 \times 10^9$ /L, was documented in 33 (32.35%) patients. None of the patients evaluated had haemoglobin of less than 8 g/L and/or haemolytic anaemia secondary to *M. pneumoniae* infection.

Comparison of laboratory tests results among different age groups (Table 2) showed that children in the  $< 5$  yrs group had a higher number of lymphocytes ( $p < 0.0001$ ) and monocytes ( $p = 0.009$ ). Also thrombocytosis was more frequent in preschool-aged ( $p = 0.013$ ). Serum C-reactive protein was also measured in all patients: 77% had an increased level of



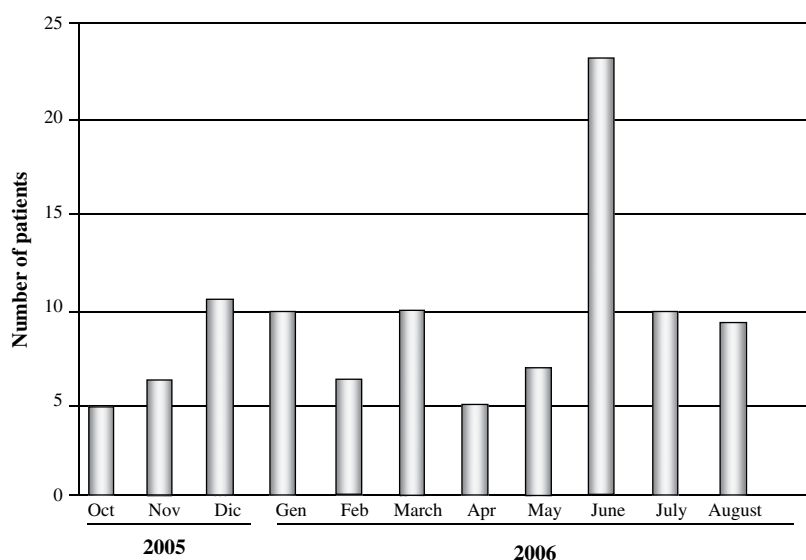
**Figure 1** Number of children admitted for an acute lower respiratory tract disease with positive polymerase chain reaction (PCR) for *M. pneumoniae* in the different age groups. The number of children evaluated is expressed on the ordinate and the different age groups on the abscissa.

more than 0.5 g/L (minimum-maximum values: 0.68-22.21 mg/dl, median: 1.55 mg/dl). IgG and IgM antibodies against *M. pneumoniae* were quantitatively detected in 83 serum samples by using the ELISA. test were analyzed Elevated serum levels of *M. pneumoniae*-specific IgM and/or IgG, confirming a diagnosis of *M. pneumoniae* infection, were detected in 38 (45.8%) on admission (Table 3). In patients with negative serology, a "convalescent" sample was obtained and showed in all patients an elevation of *M. pneumoniae*-specific IgM and/or IgG levels (>30 U/ml and >17 U/ml, respectively) consistent with a recent *M. pneumoniae* infection.

Co-infections with RSV occurred in 4 children younger than 2 yrs.

#### Characteristics of *M. pneumoniae* infection in patients less than 1 yr of age

In the ≤2 yrs group, 8 infants had ≤8 months of age, (two 1 month old, one 4 months old, two 5, one 6 and two 8 months old, respectively) and, in addition to a positive PCR for *M. pneumoniae*, three had also detectable antigen-specific IgM and IgG in serum. Transcutaneous oxygen saturation in room air was <95% only in two patients and, in addition to respiratory symptoms, three presented vomiting. Chest X-ray was reported as abnormal in all but one infant (6 had interstitial changes and two parenchymal consolidations) while co-infections with RSV occurred in three cases (Table 4).



**Figure 2** Number of children with positive polymerase chain reaction (PCR) for *M. pneumoniae*, admitted for an acute lower respiratory tract disease in the period October 2005-August 2006. The number of children evaluated is expressed on the ordinate and the different months when admission was performed on the abscissa.

**Table 1** Comparison of clinical features of *Mycoplasma pneumoniae* infection among different age groups

	<5 yrs (No. 39)	5–<10 yrs (No. 42)	≥10 yrs (No. 21)	p-Value
Fever [No. (%)]	27 (69.23%)	34 (80.95%)	14 (66.67%)	0.36
Wheezing [No. (%)]	13 (33.33%)	12 (28.57%)	11 (52.38%)	0.17
Cough [No. (%)]	19 (48.72%)	31 (73.81%)	12 (57.14%)	0.06
Dyspnoea [No. (%)]	18 (46.15%)	6 (14.28%)	4 (19.05%)	0.004
Diarrhoea [No. (%)]	3 (7.69%)	2 (4.76%)	0 (0)	0.53 <sup>a</sup>
Coriza [No. (%)]	9 (23.08%)	5 (11.90%)	1 (4.76%)	0.16 <sup>a</sup>
Vomiting [No. (%)]	8 (20.51%)	5 (11.90%)	2 (9.52%)	0.51 <sup>a</sup>
SaO <sub>2</sub> < 97% [No. (%)]	15 (38.46%)	15 (35.71%)	6 (28.57%)	0.60
Crackles [No. (%)]	12 (30.77%)	20 (47.62%)	8 (38.10%)	0.30
Consolidations [No. (%)]	14 (35.85%)	34 (80.95%)	14 (66.67%)	0.004 <sup>a</sup>
Monolateral consolidation [No. (%)]	10 (25.64%)	24 (57.14%)	9 (42.86%)	0.89 <sup>a</sup>
Bilateral consolidation [No. (%)]	4 (10.26%)	10 (23.81%)	5 (23.81%)	—
Interstitial changes [No. (%)]	11 (28.21%)	2 (4.76%)	1 (4.76%)	<0.0001 <sup>a</sup>

p-Values in the table refer to Chi-square test, unless otherwise specified.

<sup>a</sup> Fisher's Exact test.

## Discussion

Evaluating children admitted for lower respiratory tract infection (LRTI) over an 11-month period, we found that approximately 12% had a positive PCR for *M. pneumoniae* and of these, 39 were less than 5 yrs old, including 8 infants younger than 8 months of age. In all children with *M. pneumoniae* infection the commonest symptoms were cough and fever, while chest X-ray demonstrated predominantly consolidations (76% of the radiological abnormalities recorded), interstitial changes, and pleural effusions being reported, respectively, in 17 and 7%. Differences in the

clinical presentation of *M. pneumoniae* infection were detected among younger and older patients. In children less than 5 yrs old tachypnoea, upper respiratory tract involvement, diarrhoea and vomiting were more common ( $p = 0.047$ ), interstitial changes on chest X-rays were more frequently reported and laboratory test showed higher number of lymphocytes and monocytes. Thrombocytosis and co-infections with RSV were also more common in the younger than in the older patients.

*M. pneumoniae* infections have been traditionally thought to occur in school-aged children, although recent studies indicated that it may be less rare than believed in

**Table 2** Comparison of laboratory values of *Mycoplasma pneumoniae* infection among different age groups

	< 5 yrs (No. 39)	5– < 10 yrs (No. 42)	≥10 yrs (No. 21)	p-Value
White blood cells (cells/mm <sup>3</sup> )	12.88 (6.12)	10.59 (4.81)	9.60 (4.15)	0.08
Monocyte number (cells/mm <sup>3</sup> ) [mean (SD)]	0.80 (0.46)	0.65 (0.83)*	0.48 (0.17)¶	0.009
Monocytes percentage [median (lower–upper quartiles)]	6.11 (4.70–8.75)	4.65 (3.49–6.53)	5.54 (3.74–7.59)	0.17
Lymphocyte number (cells/mm <sup>3</sup> ) [mean (SD)]	4.22 (3.25)	2.26 (1.20)***	1.72 (0.58)¶¶¶	<0.0001
Lymphocyte percentage [median (lower–upper quartiles)]	35.71 (20.30–43.44)	19.65 (16.40–30.05)**	18.64 (13.10–25.98)¶¶	<0.001
Neutrophil number (cells/mm <sup>3</sup> ) [mean (SD)]	7.11 (4.71)	7.36 (4.19)	7.07 (4.09)	0.96
Neutrophil percentage [median (lower–upper quartiles)]	49.91 (41.50–69.91)	69.37 (57.75–74.93)**	71.27 (62.75–80.25)¶¶¶	<0.001
Eosinophil number (cells/mm <sup>3</sup> ) [mean (SD)]	0.30 (0.34)	0.23 (0.21)	0.21 (0.18)	0.35
Eosinophil percentage [median (lower–upper quartiles)]	1.31 (0.76–2.98)	1.91 (0.76–3.64)	1.70 (0.83–3.78)	0.84
Platelet number (cells/mm <sup>3</sup> ) [mean (SD)]	409.8 (150.6)	334.7 (114.1)*	316.6 (90.84)¶	0.009
Serum C-reactive protein (mg/dl) [median (lower–upper quartiles)]	0.89 (0.46–2.24)	1.64 (1.24–3.40)	2.09 (0.83–3.56)	0.69

¶  $p < 0.05$ , comparison between age group 1 and age group 3; ¶¶  $p < 0.01$ , comparison between age group 1 and age group 3;

¶¶¶  $p < 0.001$ , comparison between age group 1 and age group 3; \*  $p < 0.05$ , comparison between age group 1 and age group 2;

\*\*  $p < 0.01$ , comparison between age group 1 and age group 2; and \*\*\*  $p < 0.001$ , comparison between age group 1 and age group 2.



**Table 3** Age-dependent distribution of *Mycoplasma pneumoniae* infection on the basis of serological and PCR findings at admission

	<5 yrs (No. 39)	5–<10 yrs (No. 42)	≥10 yrs (No. 21)
Antigen-specific IgM [No. (%)]	9 (23.08)	21 (50.00)	6 (28.57)
Antigen-specific IgG [No. (%)]	5 (12.8)	13 (30.95)	4 (19.05)
PCR [No. (%)]	39 (100.00)	42 (100.00)	21 (100.00)

children less than 5 yrs old.<sup>6,8,9,13</sup> Indeed, reports from different countries indicate that the incidence of *M. pneumoniae* is highest, in school-aged children, but also in children 1–5 yrs of age, but with infants less than 1 yr old were rarely affected.<sup>6,8,9,13,14</sup> The results here reported are only partially in agreement with the other studies since out of the 102 children with *M. pneumoniae* infection, 42 were between 5 and 10 yrs of age and 21 between 10 and 14 yrs of age, but 39 were less than 5 yrs old, including 8 young infants.

Indeed, in the study performed in Finland, but only on patients with community-acquired pneumonia, only 21% of the children with *M. pneumoniae* infection were <5 yrs of age, a percentage similar to the 18% reported during the epidemic outbreak in Catalonia,<sup>7</sup> while in the Australian study, out of the children presenting to a tertiary children's hospital with *M. pneumoniae* infection, 39% were less than 5 yrs old.<sup>9</sup>

The relatively low incidence in adolescents, found in the present but also in other reports,<sup>9</sup> may be probably explained by the observation that among persons who have had *M. pneumoniae* infection, rates of subsequent relapse are low because immunity appears to increase progressively with age.<sup>14</sup>

Unlike endemic disease, which may not demonstrate marked seasonal occurrence, it is generally thought that outbreaks of *M. pneumoniae* infection in countries with

temperate climates, such as Italy, tend to occur in the summer or early fall, when the occurrence of other respiratory pathogens is generally lower.<sup>15</sup> Although we have observed a peak incidence in June, with a total of 23 cases out of a total of 102, *M. pneumoniae* infection occurred throughout all the period evaluated, with 12 and 99 cases, respectively, in December and January.

To select children with *M. pneumoniae* infection at enrolment, positivity of PCR on throat swab specimen, an approach thought to be highly sensitive and specific was considered.<sup>16,17</sup> Indeed, lack of antibody response to *M. pneumoniae* has been noted in both paediatric and adult populations with culture- and/or PCR-positive community-acquired pneumonia<sup>18</sup> and nonspecific stimulus by lipids of other organisms may lead to production of crossreacting antibodies.<sup>14</sup> The diagnosis of *M. pneumoniae* infection was then confirmed by the presence of elevated serum levels of *M. pneumoniae*-specific IgM and/or IgG, in the acute phase or their increase in the convalescent phase.

The clinical presentation observed in our patient population did not differ greatly from that described in other studies,<sup>1,2,7</sup> fever and cough being the most common symptoms. Despite the hospital-based nature of our study, the rate of acute dyspnoea and wheezing was lower than recently reported in a similar series.<sup>9</sup> Consistent with the results of this latter study, we found a significant difference in clinical features between the younger and older children with *M. pneumoniae* infection, dyspnoea, upper respiratory tract involvement, diarrhoea and vomiting being more common in the less than 5 yrs old group than in the other two groups.

A high proportion of children had a chest roentgenograms reported as abnormal, but without pathognomonic features: segmental or patchy consolidation was common in the whole population studied, as in other series,<sup>6,19</sup> while interstitial changes were more often reported in the youngest group. Pleural effusion was a relatively rare finding and hilar or mediastinal lymphadenopathy was never detected.<sup>6,19,20</sup> The observation that the present study was performed on children presenting and admitted to a tertiary children's hospital may also explain the high

**Table 4** Clinical features of *Mycoplasma pneumoniae* infection in children less than 8 months of age

Pt ID	Age (yrs)	Sex	Clinical presentation	Chest auscultation	SaO <sub>2</sub> (%)	Temperature (°C)	Chest X-ray	Co-infection
1	0.30	F	Coryza, cough and vomiting	Bronchial breathing	99	36.8	Bilateral consolidation	None
2	0.44	M	Fever	Crackles and wheeze	100	38.5	Interstitial changes or interstitial infiltrates	RSV
3	0.12	F	Vomiting	Crackles	98	36.8	Interstitial changes or interstitial infiltrates	None
4	0.12	M	Cough	Crackles	100	37.6	Interstitial changes or interstitial infiltrates	None
5	0.54	F	Cough Tachydyspnoea	Wheeze	99	36.5	Interstitial changes or interstitial infiltrates	None
6	0.42	F	Tachydyspnoea	Wheeze	94	36.3	Normal	RSV
7	0.69	F	Cough	Wheeze	93	36.7	Interstitial changes or interstitial infiltrates	None
8	0.64	M	Fever	Bronchial breathing	97	39.2	Unilateral consolidation	RSV

proportion of cases with clinical and roentgenographic findings consistent with *M. pneumoniae*-induced pneumonia, as compared with milder manifestations.

Finally, preschool-aged children had a higher number of lymphocytes, monocytes and platelets. It is interesting to note that thrombocytosis has been reported only twice in children<sup>9</sup> and in elderly adults.<sup>21</sup>

In conclusion, consistent with other studies, these results emphasize the concept that *M. pneumoniae* should be kept in mind as a cause not only of community-acquired pneumonia, but also of milder respiratory infections in children less than 5 yrs old. Indeed, *M. pneumoniae* may cause not only pneumonia but also other respiratory syndromes such as bronchitis, bronchiolitis, mimicking viral respiratory infections.

## Conflict of interest

The authors have declared no conflict of interest.

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## References

- Cherry J, Ching N. *Mycoplasma* and *Ureaplasma* infections. In: Feigin RD, Cherry DJ, editors. *Textbook of pediatric infectious diseases*. 5th ed. Pennsylvania: W.B. Saunders; 2004. p. 2516–47.
- Hammerschlag M. *Mycoplasma pneumoniae* infections. *Curr Opin Infect Dis* 2001;14(2):181–6.
- Korppi M, Heiskanen-Kosma T, Jalonen E, Saikku P, Leinonen M, Halonen P, et al. Aetiology of community-acquired pneumonia in children treated in hospital. *Eur J Pediatr* 1993;152(1):24–30.
- Clyde WJ. *Mycoplasma pneumoniae* respiratory disease symposium: summation and significance. *Yale J Biol Med* 1983;56(5–6):523–7.
- Principi N, Esposito S, Blasi F, Allegra L. Role of *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* in children with community-acquired lower respiratory tract infections. *Clin Infect Dis* 2001;32(9):1281–9.
- Waris M, Toikka P, Saarinen T, Nikkari S, Meurman O, Vainionpää R, et al. Diagnosis of *Mycoplasma pneumoniae* pneumonia in children. *J Clin Microbiol* 1998;36(11):3155–9.
- Domínguez A, Minguell S, Torres J, Serrano A, Vidal J, Salleras L. Community outbreak of acute respiratory infection by *Mycoplasma pneumoniae*. *Eur J Epidemiol* 1996;12(2):131–4.
- Bosnak M, Dikici B, Bosnak V, Dogru O, Ozkan I, Ceylan A, et al. Prevalence of *Mycoplasma pneumoniae* in children in Diyarbakir, the south-east of Turkey. *Pediatr Int* 2002;44(5):510–2.
- Othman N, Isaacs D, Kesson A. *Mycoplasma pneumoniae* infections in Australian children. *J Paediatr Child Health* 2005;41(12):671–6.
- Wang EEL, Long SS. Acute uncomplicated pneumonia. In: Long SS, Pickering LK, Prober CG, editors. *Principles and practice of pediatric infectious diseases*. New York: Churchill Livingstone; 1997. p. 250–7.
- Ruuskanen O, Ogra PL. Respiratory syncytial virus. *Curr Probl Pediatr* 1993;23:50–79.
- Di Marco E, Cangemi G, Filippetti M, Melioli G, Biassoni R. Development and clinical validation of a real-time PCR using uni-molecular Scorpion-based probe for the detection of *Mycoplasma pneumoniae* in clinical isolates. *New Microbiol* 2007;30(4):415–21.
- Pönkä A, Ukkonen P. Age-related prevalence of complement-fixing antibody to *Mycoplasma pneumoniae* during an 8-year period. *J Clin Microbiol* 1983;17(4):571–5.
- Foy H. Infections caused by *Mycoplasma pneumoniae* and possible carrier state in different populations of patients. *Clin Infect Dis* 1993;17(Suppl. 1):S37–46.
- Waites K. New concepts of *Mycoplasma pneumoniae* infections in children. *Pediatr Pulmonol* 2003;36(4):267–78.
- Ramirez J, Ahkee S, Tolentino A, Miller R, Summersgill J. Diagnosis of *Legionella pneumophila*, *Mycoplasma pneumoniae*, or *Chlamydia pneumoniae* lower respiratory infection using the polymerase chain reaction on a single throat swab specimen. *Diagn Microbiol Infect Dis* 1996;24(1):7–14.
- Kai M, Kamiya S, Yabe H, Takakura I, Shiozawa K, Ozawa A. Rapid detection of *Mycoplasma pneumoniae* in clinical samples by the polymerase chain reaction. *J Med Microbiol* 1993;38(3):166–70.
- Block S, Hedrick J, Hammerschlag M, Cassell G, Craft J. *Mycoplasma pneumoniae* and *Chlamydia pneumoniae* in pediatric community-acquired pneumonia: comparative efficacy and safety of clarithromycin vs. erythromycin ethylsuccinate. *Pediatr Infect Dis J* 1995;14(6):471–7.
- Stevens D, Swift P, Johnston P, Kearney P, Corner B, Burman D. *Mycoplasma pneumoniae* infections in children. *Arch Dis Child* 1978;53(1):38–42.
- Fine N, Smith L, Sheedy P. Frequency of pleural effusions in mycoplasma and viral pneumonias. *N Engl J Med* 1970;283(15):790–3.
- Marmion B, Williamson J, Worswick D, Kok T, Harris R. Experience with newer techniques for the laboratory detection of *Mycoplasma pneumoniae* infection: Adelaide, 1978–1992. *Clin Infect Dis* 1993;17(Suppl. 1):S90–9.